

IN THE CLAIMS

Please amend the Claims as follows:

1. (original) A method of modulating splice site selection and splicing thereof, said method comprising the step of hybridizing an oligonucleotide-protein conjugate to a target pre-mRNA molecule in a cell or cell extract, wherein said oligonucleotide-protein conjugate comprises an oligonucleotide moiety capable of binding to a protein moiety which comprises at least two distinct sequence elements:

(i) a nucleic acid sequence that is complementary to a specific region upstream of said splice site in said target pre-mRNA molecule; and

(ii) an extension containing a protein binding site sequence element for covalently binding a protein; and

wherein said protein moiety comprises a protein capable of modulating splicing of said splice site upon binding with said protein binding site.

2. (currently amended) The method of claim 1, wherein said binding of said protein is effected prior to hybridizing of said oligonucleotide moiety to said target pre-mRNA molecule or thereafter.

3. (original) The method of claim 1, wherein said modulating is one of increasing or repressing splice site selection and splicing thereof.

4. (original) The method of claim 1, wherein said splice site is a 5' splice site.

5. (original) The method of claim 1, wherein said splice site is a 3' splice site.

6. (original) The method of claim 1, wherein said cell is a mammalian cell.

7. (currently amended) The method of claim 1~~m~~₂, wherein said cell is in a patient.

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27. (canceled)

28. (original) The method of claim 1, wherein said oligonucleotide moiety is having a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2 to SEQ ID NO:14 and SEQ ID NO:18 to SEQ ID NO:33.

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84. (canceled)

85. (original) An oligonucleotide moiety for modulating splice site selection and splicing thereof in a target pre-mRNA molecule present in a cell or cell extract, which comprises at least two distinct sequence elements:

(i) a nucleic acid sequence that is complementary to a specific region upstream of said splice site in said target pre-mRNA molecule; and

(ii) an extension containing a protein binding site sequence element for covalently binding a protein.

86. (original) The oligonucleotide moiety of claim 85, wherein said extension is 5' CGU ACA CCA

UCA GGG UAC-3' (SEQ ID NO: 1).

87. (currently amended) The oligonucleotide moiety of claim ~~83~~ 85, wherein said oligonucleotide moiety is comprising a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2 to SEQ ID NO:14 and SEQ ID NO:18 to SEQ ID NO:33.

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102. (canceled)

103. (canceled)

104. (currently amended) A method of creating an alternate form of mRNA or an alternate form of a protein comprising the steps of administering to a cell or a cell extract a sufficient amount of the oligonucleotide moiety of ~~any one of claim[[s]] 85 to 103~~ and administering to said cell or said cell extract a purified protein capable of binding to said protein binding site.

105. (canceled)

106. (canceled)

107. (currently amended) A method of reducing and/or inhibiting expression of an mRNA molecule or protein, said method comprising the step of administering to a cell or a cell extract a sufficient

amount of the oligonucleotide moiety of ~~any one of claim[[s]] 85 to 103~~ and administering to said cell or said cell extract a purified protein capable of binding with said protein binding site.

108. (currently amended) A method of reducing and/or inhibiting neuronal differentiation, said method comprising the steps of administering to a cell or a cell extract a sufficient amount of the oligonucleotide moiety of ~~any one of claim[[s]] 85 to 103~~ and administering to said cell or said cell extract a purified protein capable of binding with said protein binding site.

109. (currently amended) A method of preventing a viral infection in a patient, said method comprising the step of administering a therapeutically effective amount of the oligonucleotide moiety of ~~any one of claim[[s]] 85 to 103~~ and a therapeutically effective amount of a purified protein capable of binding with said protein binding site to said patient.

110. (canceled)

111. (canceled)

112. (canceled)

113. (canceled)

114. (canceled)

115. (canceled)

116. (currently amended) A method for treating a disease resulting from a mutation leading to

aberrant splicing in a patient, said method comprising the steps of administering a therapeutically effective amount of the oligonucleotide moiety of ~~any one of claim~~[[s]] 85 ~~to 103~~ and a therapeutically effective amount of a purified protein capable of binding to said protein binding site to said patient.

117. (original) The method of claim 116, wherein said disease is selected from the group consisting of β -thalassemia, cystic fibrosis, haemophilia, retinoblastoma, analbuminemia, Lesch-Nyhan syndrome, acute intermittent porphyria, breast and ovarian cancer, carbohydrate-deficient glycoprotein syndrome type 1a, cerbrotendinous xanthomatosis, Ehlers-Danlos syndrome type VI, Fanconi anemia, frontotemporal dementia, HPRT deficiency, Leigh's encephalomyelopathy, Marfan syndrome, metachromatic leukodystrophy (juvenile form), neurofibromatosis type 1, OCT deficiency, porphyria cutanea tarda, Sandhoff disease, severe combined immunodeficiency, spinal muscle atrophy, tyrosinemia type 1, and Duchenne muscular dystrophy.

118. (canceled)

119. (canceled)

120. (canceled)

121 (canceled)

122. (canceled)

123. (currently amended) A method for promoting cell death in a patient, said method comprising the steps of administering an effective amount of the oligonucleotide moiety of ~~any one of claim~~ 85 ~~to 103~~ and an effective amount of a purified protein capable of binding to said protein binding site to

said patient.

124. (canceled)

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126. (canceled)

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128. (canceled)

129. (canceled)

130. (currently amended) A method for preventing and/or reducing the growth of tumor cells in a patient, said method comprising the steps of administering a therapeutically effective amount of the oligonucleotide moiety of ~~any one of claim~~[[s]] 85 ~~to 103~~ and a therapeutically effective amount of a purified protein capable of binding with said protein binding site to said patient.

131. (original) The method of claim 130, wherein said tumor cells are selected from the group consisting of lung cancer cells, liver cancer cells, pancreatic cancer cells, brain cancer cells, colon cancer cells, kidney cancer cells, bone cancer cells, breast cancer cells, prostate cancer cells, uterine cancer cells, lymphoma cells, melanoma cells, myeloma cells, adenocarcinoma cells, thymoma cells and plasmacytoma cells.

132. (canceled)

133. (canceled)

134. (canceled)

135. (canceled)

136. (canceled)

137. (canceled)

138. (currently amended) A composition comprising the oligonucleotide moiety of ~~any one of~~ claim[[s]] 85 to 103 in association with a pharmaceutically acceptable carrier.

139. (new) The method of claim 85 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is covalently attached to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

140. (new) The method of claim 104 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is covalently attached to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

141. (new) The method of claim 107 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is covalently attached to a

protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

142. (new) The method of claim 108 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is covalently attached to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

143. (new) The method of claim 109 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is covalently attached to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

144. (new) The method of claim 116 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is covalently attached to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

145. (new) The method of claim 123 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is covalently attached to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

146. (new) The method of claim 130 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is covalently attached to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

147. (new) The method of claim 108 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is covalently attached to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.

148. (new) The composition of claim 138 wherein said oligonucleotide moiety comprises an oligonucleotide protein conjugate in which said oligonucleotide moiety is covalently attached to a protein moiety, and said protein moiety comprises a protein capable of modulating splicing of said splice site.